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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,082	12/11/2003	James G. Lazar	2629-4036	1602

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EXAMINER	
BRUSCA, JOHN S	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 04/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/735,082	LAZAR ET AL.	
	Examiner	Art Unit	
	John S. Brusca	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-22 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-22 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3/8/2006.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

1. The information disclosure statement filed 11 December 2003 fails to comply with 37 CFR 1.98(a)(1), which requires the following: (1) a list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) U.S. patents and U.S. patent application publications listed in a section separately from citations of other documents; (3) the application number of the application in which the information disclosure statement is being submitted on each page of the list; (4) a column that provides a blank space next to each document to be considered, for the examiner's initials; and (5) a heading that clearly indicates that the list is an information disclosure statement. The information disclosure statement has been placed in the application file, but the information referred to therein has not been considered. The statement is a paper from parent Application No. 09/707178, rather than a paper for the instant application.

2. The Information Disclosure Statement filed 08 March 2006 has been considered in its entirety and a signed list of references is attached to this Office action. It is noted that the Information Disclosure Statement filed 08 March 2006 comprises all references listed in the copy of the Information Disclosure Statement of parent Application No. 09/707178 discussed above.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-9 and 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-9 are indefinite because it is not clear if the antibody binds to the first or the second of the two RNA DNA hybrids, or whether the antibody binds to both RNA DNA hybrids.

Claims 13-15 are indefinite because the role of the microarray bound biomolecule of step (b) is in the claimed method.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Coutlee et al. (Anal. Biochem, Vol. 181, pages 153-162 (1989), reference 25 in the Information Disclosure Statement filed 08 March 2006).

The claims are drawn to a method of hybridizing an RNA DNA hybrid in which one strand is derivatized, followed by binding the hybrid to an array comprising a molecule that binds the derivatized strand. The hybrid is then bound by an RNA DNA specific labeled antibody.

Coutlee et al. shows in figure 1 a model of a method of binding an RNA DNA hybrid in which the DNA strand comprises biotin, and the hybrid is bound to wells of a microtiter plate

coated with anti-biotin antibody. The hybrid is then assayed by use of a labeled antibody that is specific for RNA DNA hybrids.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coutlee et al.

The claims are drawn to a method of hybridizing an RNA DNA hybrid in which one strand is derivatized, followed by binding the hybrid to an array comprising a molecule that binds the derivatized strand. The hybrid is then bound by an RNA DNA specific labeled antibody. In some embodiments the assay is repeated for different samples either sequentially or simultaneously.

Coutlee et al. shows in figure 1 a model of a method of binding an RNA DNA hybrid in which the DNA strand comprises biotin, and the hybrid is bound to wells of a microtiter plate coated with anti-biotin antibody. The hybrid is then assayed by use of a labeled antibody that is specific for RNA DNA hybrids. Coutlee et al. shows analysis of multiple samples in the methods section and throughout. Coutlee et al. does not show repetition of the assay specifically either sequentially or simultaneously.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Coutlee et al. by repeating the assay either sequentially or simultaneously because Coutlee et al. shows analysis of multiple samples and repetition of assays must be done either simultaneously or sequentially.

10. Claims 16-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carrico (U.S. Patent No. 5,200,313, reference 4 in the Information Disclosure Statement filed 08 March 2006) in view of Lockhart et al. (reference 33 in the Information Disclosure Statement filed 08 March 2006) in view of WO 93/10263 (Diagene Diagnostics Inc.) (reference 12 in the Information Disclosure Statement filed 08 March 2006).

The claims are drawn to a kit comprising the a nucleic acid array, a labeled antibody specific for RNA-DNA hybrids, hybridization and wash buffers, and Rnase. In some embodiments the antibody is monoclonal or polyclonal

Carrico shows assay of hybrids by use of RNA:DNA hybrid-specific antibodies in the abstract. Carrico shows methods in which the probe is attached to a support in figure 1 and methods in which the probe is in solution prior to hybridization and is attached to a support by a biotin moiety subsequent to hybridization in figure 2. Carrico shows in column 2 that use of

antibody labeling of RNA:DNA hybrids allows for elimination of nucleic acid labeling steps. Carrico shows in column 7 that the probe may be attached to solid supports such as nitrocellulose membranes. Carrico shows that the RNA:DNA hybrid specific antibodies may be polyclonal or monoclonal in column 10. Carrico does not show use of arrays of probes or RNase.

Lockhart et al. shows DNA arrays and methods of using the arrays to assess many different mRNA levels. Lockhart et al. shows on page 1675 arrays with a density of greater than 16,000 probes per 1.6 cm^2 (> 10,000 probes per 1 cm^2). Lockhart et al. shows on page 1676 that the probes are 20mers. Lockhart et al. shows on page 1676 that the use of short probes allows for increased resolution of information about the sample, for example by detecting alternatively spliced mRNA and to differentiate between closely related members of gene families.

Diagene Diagnostics Inc. shows that assays of RNA DNA hybrids are facilitated by use of RNase to digest non hybridized probe on page 11.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Carrico by use of the high density array of short probes of Lockhart et al. because Lockhart et al. shows that their array has advantages in the detection of information about alternatively spliced mRNA and expression levels of closely related members of gene families. It would have been further obvious to treat the hybridized samples with RNase to facilitate removal of unhybridized probe as taught by Diagene Diagnostics Inc.

Conclusion

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the

USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center at (800) 786-9199.Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, PhD. can be reached on 571 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

16 April 2006

John S. Brusca
Primary Examiner
Art Unit 1631

jsb